Ex Vivo Gene Editing of Human Hematopoietic Stem Cells for the Treatment of X-Linked Hyper-IgM Syndrome

Grant Award Details

Ex Vivo Gene Editing of Human Hematopoietic Stem Cells for the Treatment of X-Linked Hyper-IgM Syndrome

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-11536

Investigator:

Name:	Caroline Kuo
Institution:	University of California, Los Angeles
Type:	PI

Disease Focus: Blood Disorders, Hyper IgM Syndrome, Immune Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: $4,896,628

Status: Pre-Active

Grant Application Details

Application Title: Ex Vivo Gene Editing of Human Hematopoietic Stem Cells for the Treatment of X-Linked Hyper-IgM Syndrome

Public Abstract:

Translational Candidate

Human hematopoietic stem cells that have been gene-corrected at the CD40L gene to treat patients with X-Linked Hyper-IgM Syndrome

Area of Impact

These studies will bring stem cell gene therapy for XHIM closer to the clinic especially those without an HLA match or infections too severe for HSCT.

Mechanism of Action

The CRISPR/Cas9 platform allows site-specific integration of a corrective copy of the CD40L gene at its normal location, maintaining expression of the corrective DNA under control of natural regulatory elements. Transplantation of gene-corrected hematopoietic stem cells, which are self-renewing and long-lived, produces all blood lineages, including T lymphocytes with restored CD40L expression than can stimulate B cells to produce class-switched immunoglobulin.

Unmet Medical Need

There is no curative treatment for XHIM patients without a bone marrow match or with severe infections. Gene corrected HSC can cure XHIM and provides a therapeutic option for these patients. This proposal will advance the field of stem cell gene therapy and treatment of primary immunodeficiencies.

Project Objective

Pre-IND meeting

Major Proposed Activities

- Characterize clinical grade critical reagents in healthy and XHIM hematopoietic stem cells. Perform clinical scale run and pilot toxicology study.
- Assess off-target insertions and deletions caused by CRISPR/Cas9 in additional cell lines and in primary hematopoietic stem cells.
- Prepare clinical protocol, investigator's brochure, consent forms, and Pre-IND package. Complete Pre-IND meeting with the FDA.

Statement of Benefit to California:

Safe, definitive therapies for XHIM represent an unmet medical need. Allogeneic stem cell transplant is frequently complicated by graft-versus-host disease and worsening of pre-existing infections. Successful demonstration that stem cell gene therapy can safely and effectively cure XHIM will shift the paradigm by which patients will be treated, led by California's position as a leader in the field of gene therapy. This will result in improved patient care in the state and around the world.

Source URL: https://www.cirm.ca.gov/our-progress/awards/ex-vivo-gene-editing-human-hematopoietic-stem-cells-treatment-x-linked-hyper-igm